Remarks

Claims 1-5 are presently being examined. Claims 6-60 have been withdrawn by the Examiner as being drawn to non-elected inventions and have been canceled by the above amendment. New claim 61 has been added by this amendment.

Amendments to the Claims

Claims 6-60 have been canceled by the foregoing amendment in conformity with the previous restriction requirement since those claims are directed to non-elected subject matter. Applicants reserve the right to file a divisional application directed to the subject matter of claims 6-60. New claim 61 was added by this amendment. New claim 61 is supported by original claim 5 and in the specification at, for example, page 15, lines 22-27. No new matter has been added by this amendment. Entry of the above amendments and reconsideration and withdrawal of the rejections of claims 1-5 is respectfully requested.

35 U.S.C. §103(a) Rejection of Claims 1-5

Claims 1-5 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over MacLean et al. and Lund et al. The Examiner has alleged that MacLean discloses that an estrogen agonist/antagonist is useful for treating andropause and that Lund et al. discloses that testosterone is useful for treating andropause. The Examiner then alleged that the combination of MacLean and Lund renders the presently claimed method obvious. Applicants respectfully traverse.

The combination of MacLean et al. and Lund et al. does not teach or suggest to one skilled in the art the claimed invention, which relates to methods of treating male andropause using a combination of an estrogen agonist/antagonist and testosterone. Nor does the combination of MacLean et al. and Lund et al provide a reasonable expectation of success that a combination of an estrogen agonist/antagonist and testosterone could be used to treat male andropause.

The combination of MacLean et al. and Lund et al. is deficient because nowhere in MacLean et al. is the treatment of male andropause even mentioned. Instead, MacLean et al. recites treatment of testosterone deficiency, which is different from andropause. Andropause in men, like menopause in women, occurs later in life, and has a number of biological consequences. Moreover, nowhere in MacLean et al. is there any suggestion to combine an estrogen agonist/antagonist with testosterone. Furthermore, MacLean et al. discuss at column 13, lines 19-22, that testosterone in men is aromatized in fat, which leads to increased estrogen and that

the increase in estrogen can result in negative feedback that reduces the total testosterone levels.

The Lund et al. article does not supply the elements of the claimed invention that are missing from MacLean et al. The Lund et al. article does not even mention the use of a SERM to treat andropause. Lund et al. discusses the use of testosterone alone as a possible treatment of andropause. Applicants note that even the use of testosterone as testosterone replacement therapy (TRT) for andropause is speculative, as is shown by the last two sentences of the article on page 995.

> Because of insufficient evidence, particularly regarding psychologic safety and efficacy, general TRT in elderly hypogonadal men is not warranted. However, further clinical evaluation of TRT in men with low testosterone levels and symptoms of andropause is warranted.

Lund et al. also noted in the abstract on page 951 that the causal relationship between declining testosterone levels and development of andropause symptoms is not firmly established. Lund et al. goes on to state at page 952, right column, lines 13-16, in reference to testosterone levels, that "It also may be argued that declining levels and andropause-like symptoms occur simultaneously but share no causal relationship. Lund et al. further states that declining levels of circulating testosterone are a potential cause of symptoms but eventually concludes "additional scientific research in this area is necessary." Thus, the Lund et al. article is simply an invitation to experiment.

Lund et al. also discuss that "increasing concentrations of testosterone inhibits further secretion of GnRH through a negative feedback mechanism (See page 952, first full paragraph). GnRH, the common abbreviation for gonadotropin-releasing hormone, acts on the pituitary gland and stimulates the production of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and leads to endogenous sex steroid production (see Merck Manual, page 2385-2386 and Veldhuis, J.D. et al., Physiological Basis of Aging and Geriatrics (3rd Edition), 2003, 213-231, CRC Press LLC, Boca Raton, FL, Abstact only). Thus, administration of exogenous testosterone can negatively impact the production of endogenous testosterone due to the resulting decrease in GnRH and resultant negative feedback. The suppression of endogenous testosterone levels by administration of exogenous testosterone has been previously studied by Fujioka et al. Life Sciences, 1987, 41, 945-949. Because of the complex negative feedback mechanisms relating to the endogenous production of testosterone as recognized in both MacLean et al. and Lund et al. as well as Veldhuis et al. and Fujioka et al., it is not obvious to one skilled

in the art that andropause could be treated using a combination of an estrogen agonist/antagonist and testosterone. In other words, the combination of MacLean et al. and Lund et al. do not provide a reasonable expectation of success to one skilled in the art. Thus, the combination of MacLean et al. and Lund et al. merely provide one skilled in the art with an invitation to experiment.

Because the combination of MacLean et al. and Lund et al. do not teach or suggest the treatment of andropause using a combination of an estrogen agonist/antagonist and testosterone, nor do they provide one skilled in the art with a reasonable expectation of success in view of the complex negative feedback mechanisms involving estrogen and testosterone, Applicants submit that the presently claimed invention is patentable over MacLean et al. in view of Lund et al. For this reason applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-5.

Conclusion

Applicants believe that in view of the remarks and amendments made above, this application is in condition for allowance.

Date: 15 MARCH 2004

By:

John A. Wichtowski
Registration No. 48,032
Pfizer Inc
Legal Division
Patent Department
MS: 8260-1611
Eastern Point Road
Groton, CT 06340
Phone: (860) 715-6645
Fax: (860) 441-5221